

Program Aimed at Eradication of Tuberculosis

EDWARD T. BLOMQUIST, M.D.

FIVE YEARS ago it would have seemed unlikely that in 1963 eradication of tuberculosis would be a subject for practical planning. In 1958 for a few of the most favored areas, where incidence even then was very low, eradication was perhaps a reasonable ultimate goal. For most of the country it appeared to be impossible even as a remote goal. We were still smarting then from the effect of the study of nonhospitalized patients, which had shown that our use of the new drugs that became available early in the decade was far from satisfactory. We had come to realize that casefinding methods developed in previous years were no longer suitable, and in many areas what was happening was a sort of halfhearted continuation of chest X-ray surveys at a reduced level, plus a good deal of often aimless tuberculin testing. We were suffering from the general impression held by the keepers of some of the public purse strings and also, unfortunately, by some of our colleagues in public health, and even some of us, that the big job of tuberculosis control had been done and that what was left to do did not amount to much. The prospects were not hopeless but neither were they very encouraging, and we derived our cheer from the thought that at least there were definite downward trends.

Today the situation has changed. Death rates continue their steady decline, but case rates have been leveling off, and between 1961 and 1962 the national case rate stood still. This

does not depress me, because I feel certain it is due to improvements in the tuberculosis situation. Two things are probably affecting the case rate. First, there is greatly improved performance in the examination of contacts, which is the most fruitful of all casefinding activities. Second, the new reporting recommendations allow for more liberal and accurate counting of active primary cases; they also disallow counting cases in which activity is undetermined. Therefore, the figures reported now represent more precisely the significant cases of active disease that are occurring. This will be even more the case as the recommendations come into wider use.

My view of the leveling case rate is that it reflects a real change of mood in tuberculosis control—a change that is resulting in action that can move us forward faster. I have a very strong feeling, shared by all members of the Tuberculosis Program staff who work with State and local health departments, that there is renewed determination, energy, and spark in tuberculosis control work these days. Enthusiasm alone will not eradicate tuberculosis, but it is necessary to success, and is a good reason for thinking we can get on with it.

I do not think we are going to get rid of tuberculosis very soon. The peculiarity of the disease is such that even if we could stop all new infections right now we would still have potential cases for the future among the large number of persons who have already been infected. A couple of years ago we estimated how many people were already infected in 1960 and how long they could be expected to live. We came up with the pattern shown in figure 1. In the year 2,000 about 8 million people who

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were already infected in 1960 will still be living, plus those infected more recently. Eradicating tuberculosis is going to take time.

It will take a longer time in some areas of the country than in others. The map (fig. 2) showing the number of active cases reported in a single year, by county, gives a general idea of the geographic distribution of tuberculosis. For the workers in counties shaded black, it probably suggests that resources should be concentrated in the high-incidence areas. For those in white counties, the important thing no doubt seems to be new ways to extend the white areas. I prefer to think it allows for a pincer action, with concentration of resources in the remaining strongholds and at the same time new approaches aimed specifically at eradication converging on the problem. This allowance for diversity is another of my reasons for optimism about eradication.

My third reason is the dramatic effectiveness of present drug therapy, which makes possible recovery for more than 95 percent of all patients with active disease who receive appropriate drug therapy from the time of diagnosis. Even for patients with far-advanced cavitory disease, recovery is possible for at least 90 percent. Most patients can become bacteriologically negative within 2 to 4 months of the time their disease is first diagnosed. This potential for prompt control of communicability in itself is perhaps the most important factor in our favor.

Related to effective drug therapy is the use of drugs for prophylaxis or very early treatment, as it is called by those who have been carrying on broadscale studies of prophylactic isoniazid since 1955 (1). In each of the trials the persons taking isoniazid had much less tuberculosis than those taking placebo; that the effect was not just postponement is shown in the experience after the medication year (table 1). Isoniazid prophylaxis, when used appropriately, is clearly an important addition to tuberculosis control methods.

Four things, then, make me think we should begin to set our sights on eradication of tuberculosis: climate of the time, geographic distribution of the disease, excellence of available drug therapy, and our new tool, prophylaxis. They make it appropriate to discuss what must be done to approach eradication.

First—and it must be first everywhere—the excellent drug therapy that is available must be used so that at least 95 percent of the patients with active disease, excreting susceptible organisms, do indeed recover. This is basic, and no matter what else is done, no tuberculosis control or eradication program can succeed unless the treatment part is done well. Doing it well, in a hospital or a clinic or wherever, is a great deal more than passing out pills. It is treating sick human beings and using all the science and art of medicine to heal them. This is step number one, and it cannot be skipped.

The rest of a program aimed at eradication of tuberculosis must, I believe, be planned and executed in terms of risk of tuberculous disease. It would be inconceivable to attempt an eradication program with our present tools if everyone in the population were at equal risk. However, in the past few years, a considerable body of knowledge has been accumulating that makes it possible to define persons at risk with increasing accuracy. Applying this knowledge can speed the rate of progress toward eradication.

The persons at special risk who should probably get first attention are those who have inactive tuberculosis. There have been many studies of relapse rates over the years, with a variety of results, but all have found a relapse

Figure 1. Survival expectancy to year 2040 of the 40 million persons already infected by 1960

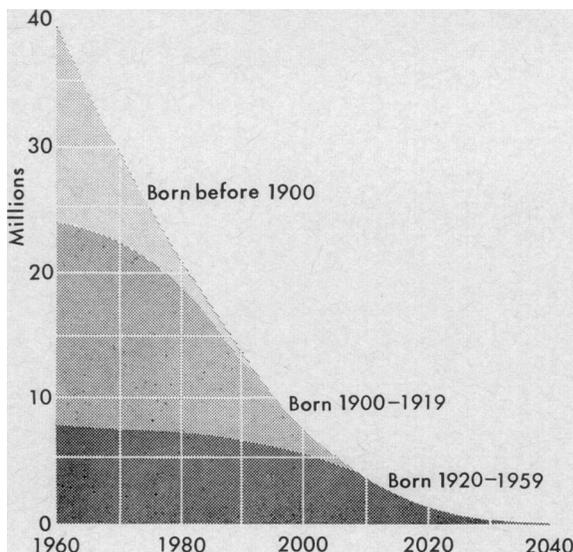
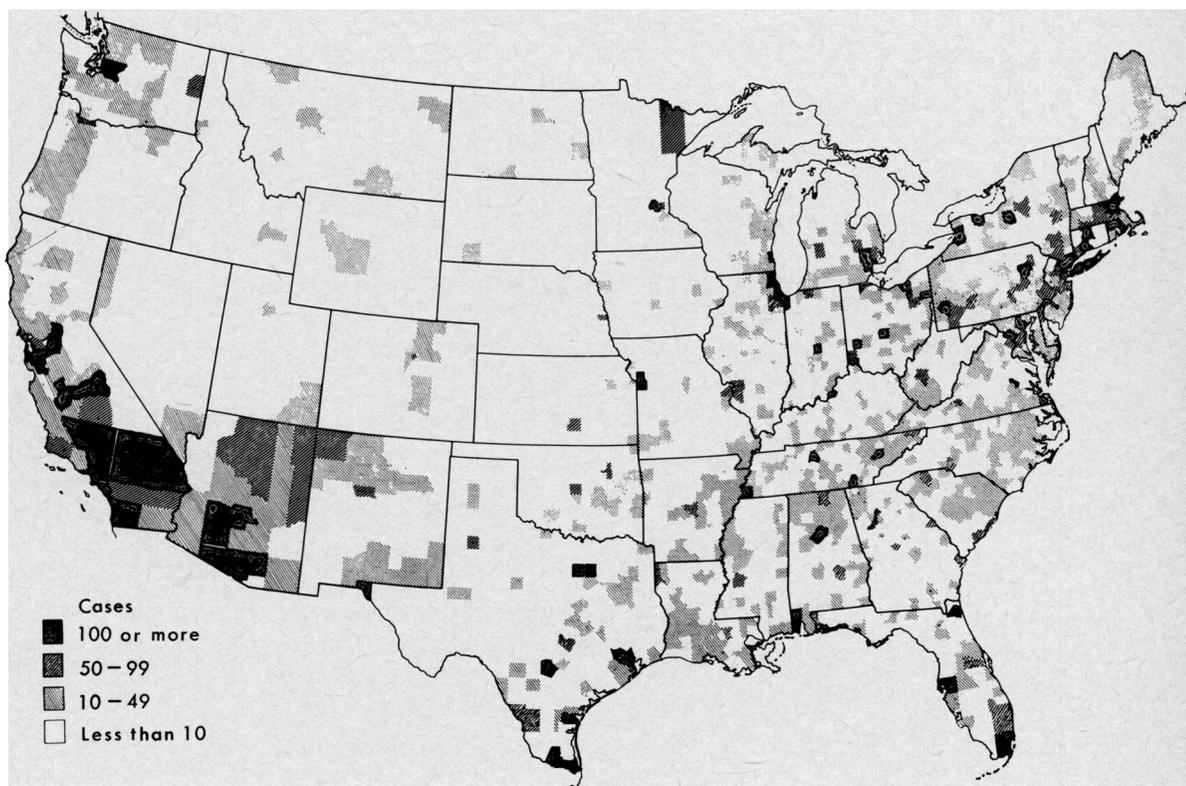


Figure 2. Distribution of new active tuberculosis cases, by county



rate high enough so that these people must be considered at high risk. Data in table 2 are from a study in Columbus, Ga., reported in 1962 (2). These figures show the numbers of reactivations of previously untreated inactive cases in the 5 years after an arbitrary date fixed at 2 years after initial diagnosis. The risk of reactivation was found to be substantial. For those who had advanced disease initially, the risk was approximately 30 percent for Negroes and 10 percent for whites. For those

under 45 years with minimal or suspected disease, it was about 15 percent for Negroes and 5 percent for whites. For older persons with minimal or suspected disease the risk was about 4 percent for Negroes and 2 percent for whites.

Table 1. Tuberculosis appearing during and after medication year

Group	Medication year		After medication year	
	Placeto	Isoniazid	Placeto	Isoniazid
Primary complications...	31	2	8	4
Contacts.....	103	26	27	18
Mental patients.....	21	4	30	15
Alaskan villagers.....	41	13	38	25

Table 2. Reactivation of inactive tuberculosis among 1,008 persons during third through seventh years after initial report as tuberculosis case or suspect

Race and initial stage of disease	Age group (years)	Number classified inactive	Number of reactivations
<i>White</i>			
Minimal and suspected...	15-44	261	11
Minimal and suspected...	45-64	412	7
Advanced.....	15-64	84	7
<i>Negro</i>			
Minimal and suspected...	15-44	128	15
Minimal and suspected...	45-64	90	3
Advanced.....	15-64	33	10
Total.....		1,008	53

From these data, it is apparent that better facilities for reexamining inactive cases will be needed than are usual in most areas.

The next high-risk group is contacts of newly reported cases. In the Public Health Service prophylaxis trials, among 25,512 household contacts of 6,219 new cases, 479 additional cases were found on initial examination (3). Table 3 shows the rates by age and ethnic group. They were very high in children under 5 in all ethnic groups. Actually, 343 of the 479 cases were in children with roentgenographic evidence of active primary tuberculosis. Overall, the "Anglos" had the lowest rates and the U.S. Spanish the highest. It seems worth pointing out that in almost every one of these age and ethnic groups, the rates of active disease found in contacts were very high in comparison with rates found in most other casefinding activities.

The remaining 25,033 contacts, those who did not have tuberculosis at the beginning, participated in the trials. About half received isoniazid and the other half placebo. Among the 12,594 who took placebo, another 107 cases developed during the year after diagnosis of the index case, giving a rate of 8.5 per 1,000—again a very high rate (table 4).

This study showed clearly that contacts of active cases have a very high risk of tuberculosis at the time the index case is diagnosed and

Table 3. Rates of active tuberculosis cases found among household contacts on initial examination, by ethnic group and age

Age group (years)	Cases per 1,000 contacts examined			
	U.S. "Anglo"	U.S. Negro	Puerto Rican	U.S. Spanish
Under 5	41	60	59	58
5-9	7	28	5	27
10-14	2	9	1	12
15-19	2	8	4	32
20-29	8	11	10	24
30-39	3	7	5	8
40-49		22	9	42
50-59	7	16	14	45
60+	5	11	18	42
All ages	10	24	15	31
Contacts examined	4,400	4,343	12,086	4,683
Cases found	42	104	187	146

Table 4. Risk of contacts developing tuberculosis during first year after diagnosis of index case, according to age

Age group (years)	Population receiving placebo	Cases	Rate per 1,000
Less than 5	2,174	28	12.9
5-9	2,570	6	2.3
10-14	2,216	10	4.5
15-19	1,262	17	13.5
20-24	651	9	13.8
25-29	549	8	14.6
30-34	588	7	11.9
35-39	553	6	10.8
40-44	468	6	12.8
45 or more	1,563	10	6.4
Total	12,594	¹ 107	8.5

¹ Pulmonary 62, extrapulmonary 16, primary 29.

Table 5. Incidence of tuberculosis among reactors and nonreactors¹

Tuberculin status on entry	Study population	Number of cases	Average annual incidence per 100,000	
			Crude	Adjusted ²
<i>Puerto Rican Trial</i>				
Total	191,827	1,149	95.3	-----
Reactors	82,269	856	163.3	165.8
Nonreactors	109,558	¹ 293	43.1	46.9
Ratio of rates			3.8	3.5
<i>Muscogee-Russell Trial</i>				
Total	64,136	216	48.2	-----
Reactors	29,369	161	78.3	67.1
Nonreactors	34,767	¹ 55	22.4	31.6
Ratio of rates			3.5	2.1

¹ With effect of vaccination removed. See reference 4.

² Adjusted to race-sex-age composition of total study population of each trial.

at least during the ensuing year. Whether they continue to be at high risk may depend on other factors.

A factor generally recognized as affecting risk is infection status. The trials of BCG vaccination conducted by the Public Health Service in Georgia, Alabama, and Puerto Rico (4) pointed up this risk. After adjustment was

made to remove the effect of the vaccine, the rates of active tuberculosis in the study populations during the 7 years after the initial testing were about three times as high for those who reacted at the beginning as for those who had no reaction (table 5).

In the household contact prophylaxis trials, the case rate was 12.3 during the first year for those in the placebo group who were infected at the beginning, and 4.9 for those uninfected at the beginning (table 6).

Roentgenographic findings constituted another factor of risk. Among 308 persons who had abnormal X-rays, 8 new cases occurred, a rate of 26 per 1,000 (table 6). The first Public Health Service prophylaxis study of extrapulmonary complications in children who reacted to tuberculin (5) also revealed a much higher risk among those who had X-ray involvement in addition (table 7). This was true for children of all ages. No complications at all occurred in children over 4 years old who had normal X-rays.

Table 8 shows the experience of a much older population, patients in mental hospitals. These data from another prophylaxis trial (6) show again that the risk of those whose X-rays showed some abnormality has been many times higher than the risk of reactors with normal X-rays. In this group, as in others, those who were uninfected at the beginning of the study

Table 6. Risk of contacts developing tuberculosis during first year after diagnosis of index case, according to infection status

Tuberculin reaction	Population receiving placebo	Cases	Rate per 1,000
Less than 5 mm.....	6, 496	32	4.9
5-9 mm.....	1, 445	12	8.3
10-14 mm.....	2, 240	23	10.3
15-19 mm.....	1, 280	16	12.5
20 or more mm.....	801	16	20.0
Abnormal roentgenogram.....	308	8	26.0
Total infected ¹	6, 074	75	12.3
Total ²	12, 594	107	8.5

¹ Includes contacts with tuberculin reactions of 5 mm. or more and those with abnormal roentgenograms.

² Includes 24 persons whose initial infection status was not established.

Table 7. Risk of extrapulmonary complications developing in tuberculin positive children during first year after entry to study, according to initial X-ray involvement ¹

Age at entry (years)	Rate per 1,000 children		
	Normal	Hilar and/or paratracheal	Parenchymal
Under 1.....	16	138	182
1-3.....	7	24	74
4-6.....	-----	18	41
7-10.....	-----	-----	-----
11 or more.....	-----	-----	133
Total.....	6	22	73

¹ Initial roentgenographic involvement found at time of entry to study.

Table 8. Tuberculosis among mental patients receiving placebo, 1 to 4 years after entrance to trial

Initial status	Population	Cases	Rate per 1,000
Uninfected.....	3, 954	4	1.0
Infected:			
Positive tuberculin.....	6, 484	24	3.7
Abnormal X-ray.....	1, 071	23	21.5

had a rather low rate, even though they were part of a population selected for study because it could be expected to have a high rate of tuberculosis.

Some of the most meticulous epidemiologic work to throw light on the matter of risk is that done by the Danish Tuberculosis Index. In this continuing study under the joint auspices of the Danish National Health Service and the World Health Organization, some 800,000 Danes, 15 years of age and older, living outside of Copenhagen were tuberculin tested and X-rayed in 1950-52. Detailed records have been kept since that time of the incidence of tuberculosis in the population that was tested. As Denmark has a relatively stable population, it was possible in almost all instances to match cases that occurred with records set up at the time of the 1950-52 campaign.

Analysis of the experience during the first 3½ to 4 years after the campaign, published in 1959 (7), showed that 76 percent of the cases occurring in that period were in persons who were unvaccinated positive reactors at the time of the campaign. This proportion, of course, was very close to that found in the Public Health Service studies in Georgia, Alabama, and Puerto Rico.

The annual rates of disease among the Danish tuberculin reactors were calculated according to X-ray findings. The rate for those with normal lungs was 27 per 100,000. In table 9, this rate is given a value of 1, to show how much greater the risk was for the persons whose X-rays showed some abnormality. Those who had suspicious shadows on the small film had a rate 14 times that of the group with normal lungs. The people with abnormal photofluorograms were called back for a roentgenogram. The lower part of the table shows a further refinement of risk in terms of the large film findings.

One problem with risk based on X-ray findings is that, because the persons at high risk are a rather small group, the larger group with normal lungs produces more cases even though their rates are much lower. The Danes analyzed the cases in the group with normal lungs, those shown in table 9 with a rate of 27 per 100,000, by age, and found that the rate in the 15- to 24-year-olds was 59 per 100,000, while the rate in the 25- to 34-year group was 32 per 100,000. Obviously, rates in older age groups were

even lower. They also found that in the group 15 to 24 years old, the size of the tuberculin reaction was related to risk. Those with a reaction of 6 to 11 mm. had a rate of 24.5. At 12 to 17 mm. the rate went up to 56.4, and at 18 to 23 mm. it went to 87.8. This greatly increased risk by size of tuberculin reaction did not occur in the older age groups.

There are, of course, other factors that increase the risk for some tuberculin reactors. In Public Health Service studies of naval recruits, Dr. Palmer and his colleagues have found that young men who were 15 percent or more underweight and were tuberculin reactors had morbidity rates four times higher than reactors who were overweight (8). The special risk of reactors who have diabetes or silicosis, or who are on long-term steroid therapy, is well known.

If we use knowingly the growing information about risk in tuberculosis control program planning, we can tailor our efforts to get the most telling effect in the long run. In working toward eradication I believe we will have to set up systems to provide examinations at intervals over long periods of time for persons at special risk. If we do this carefully, attempting only what can be done well and selecting what will be attempted on sound bases, the prospect of eradication seems quite reasonable.

With few exceptions, selection will have to be individual. We could start with the intention of seeing to it that all persons who have had tuberculosis are examined periodically for the rest of their lives. But this would undoubtedly become very difficult, probably impossible as time passed, and it would be necessary to make judgments about which cases were urgent enough to justify concentrated effort.

Contacts, it seems clear, should not only be reexamined but should receive prophylactic treatment for a year. After that year, some decision will have to be made about whether they can be discharged and forgotten or whether they should go on the list for periodic reexamination.

Beyond inactive cases and contacts, the selection could be even more difficult. Going out into the community and finding people who are at risk through tuberculin testing and chest X-rays is being attempted in some areas, and we will be watching with interest how effective

Table 9. Risk of developing disease among tuberculin reactors

Type of reading	Annual rate per 100,000 ¹	Relative value
<i>Photofluorographic</i>		
Normal lungs.....	27	1
Healed lesions.....	51	2
Suspicious shadows.....	370	14
<i>Roentgenographic</i>		
Suspicious shadows on photofluorogram:		
Normal lungs.....	50	2
Healed lesions.....	180	7
Failed to return for reading.....	500	19
Suspicious shadows.....	1,070	40

¹ In specified group.

this is. I feel, however, that there is another approach that most communities will find more practical, and that has the virtues of cutting down numbers and of providing motivation. This is an approach based on another kind of risk—not the risk to the person himself but risk to others should he develop communicable tuberculosis.

My proposal, therefore, is to concentrate our efforts on those people at personal risk who could infect children should they develop communicable tuberculosis. Eradication will have been achieved when a whole generation of children has grown up and lived out their lifetimes without becoming infected. Therefore, I propose that we select for long-term service people at risk from among those who have association with children close enough to present a potential danger of infecting them. Parents, grandparents, big sisters and brothers, cousins, aunts and uncles should be included if they are around the children very much, or the people next door if they sometimes keep the youngsters. Then there are teachers, including Sunday School and music teachers, school bus drivers, people who work in day care centers or playgrounds or camps, and babysitters or domestic workers who mind the youngsters.

What I am suggesting is not a once-in-a-while tuberculin testing and X-ray campaign for these people. It is a careful selection of those among them who are at special risk of tuberculosis and continued examinations at intervals sufficiently short so that if disease should develop it would be diagnosed early. For some of them, prophylactic treatment might be appropriate.

People will do things for children they would not be bothered to do for themselves, if they understand. Because this would be an individualized program, opportunities to explain what it was about would be built in, and these opportunities should be used carefully so that each one would feel he was contributing to the health of the children and not that he was accused of being a menace to them.

I would start by setting up a clinic specifically for the high-risk program. It could be modest at first, perhaps only weekly sessions. But it would be more than a tuberculin testing and X-ray facility. A nurse would be needed who was qualified to explain the various situa-

tions found and a physician to make the clinical judgments.

Then we could begin in the schools. We would tuberculin-test the teachers and employees, and the first grade or kindergarten. Adult reactors among the employees would be referred to the clinic for X-ray and for whatever continuing recommendations were appropriate. If any child in the first year of school reacted, his family would be asked to go to the clinic, not only for the child to get an X-ray, but for tuberculin testing and X-ray of all the adults, tuberculin testing of other children in the family, and for a full explanation of the significance of the child's reaction. At that time we would get information about other persons who were around the children enough to justify their examination also.

Finding reactors at school entrance may seem too late, but these children provide a clue to persons who could infect other children. For every child aged 6 in the United States, there are 6 children younger, and some are in the same families. Families with children tend to be associated with other families with children. Furthermore, when he first enters school the child is young enough so that trying to trace the source of his infection is not too overwhelming a job.

Certainly the way that any program of this sort was carried out would depend on the community and its services; but however it was done, it would require good facilities for examination, including medical direction. There would also have to be a record system to keep track of individual reports and recommendations and provide reminders for necessary re-examinations.

A family situation may serve to illustrate: Johnny Smith, aged 6, in the first grade, reacts to tuberculin. He lives with his mother, aged 30, his father, aged 32, and his brothers, Joe who is 8 and Sam who is 3. His paternal grandmother lives nearby and stays with the children often, as does an unmarried aunt, his mother's sister, aged 22. The source of the family's infection is found to be outside the family group. The mother and aunt and the youngest child are tuberculin negative, but father, grandmother, and older brother react. Johnny and his older brother have no signs on

their X-rays, but father and grandma do. They therefore have further X-rays and bacteriological examinations, which determine that they do not have tuberculosis. However, they are given appointments for reexamination—the father at 3 months, because of his age and the fact that he is underweight, and the grandmother at 6 months, since her age and sex place her in a less urgent risk group. In explaining the situation to the family, the physician suggests that the two older boys, who are reactors, be reexamined periodically, beginning at age 13 or 14, since the period of adolescence and young adulthood is a high-risk period for reactors. This is the first opportunity, furthermore, to begin to protect any children Johnny and Joe may have some day.

Whenever a case of tuberculosis is found in a family, the whole family is put on prophylaxis for a year, and of course is under regular supervision. At the end of the year, recommendations are made for periodic reexamination according to the risk status of the individual members—tuberculin reaction, X-ray, age, race, sex, and other pertinent factors.

At the beginning of our illustration, the school teachers and employees were examined. Two-thirds, let us suppose, are negative to tuberculin, and we can dismiss them until next year when we are again tuberculin testing first graders. The one-third who react will get chest X-rays and a detailed explanation of the significance of their tuberculin reaction. Those with negative X-rays will be put on our lists to have X-rays every year as long as they work with children. And for any who have abnormal X-rays we will provide complete diagnostic service, after which recommendations will be made in accordance with individual risk.

This program presupposes treatment facilities of a high quality and diagnostic facilities that can carry a heavier load than supporting treatment and contact programs and reexamining inactive cases. It has the advantage of being approachable a step at a time, but it could gradually be expanded to cover whole communities. It carries with it a specific message—not the vague suggestion that everybody is in danger of tuberculosis, but a positive plan to prevent tuberculous infection and especially to protect children.

This kind of program will require considerable reorientation of planning and services. It has always been said that casefinding programs were only as good as the followup. Followup was the toughest part of the job, and often it was far from adequate. Now the time has come, whether we're talking about eradication or just getting forward in tuberculosis control, when followup is truly the key, when it has to be done meticulously and for a great many more people and for long periods of time. Our old custom of screening for cases and dismissing as negative everyone who does not have active disease will no longer do. If we refine the definition of positive so that it includes the people at greatest risk as well as cases, going back to screen again will not be necessary. What is necessary is continued followup of the people at high risk so that if and when they get active disease we will be aware before they have had a chance to distribute it.

Health departments will have to be geared to provide to the risk group the necessary professional services, periodic examinations, and prophylactic drugs they provide for patients, contacts, and suspects. But they cannot be expected to undertake the continuing person-to-person work of getting people to the service. In the continuing long-term job that is ahead, if we are actually serious about eradication, the community will have to provide a great deal of help. To me, volunteer help would seem most appropriate, similar in some ways to the work of Red Cross Gray Ladies. Such volunteers could, I believe, not only help provide the personal persuasion that will be needed to motivate returns for reexamination but supplement the staff in clinics to allow professional people to give professional service. Enlisting this kind of help will be an important job of health departments undertaking an eradication program.

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American Board of Preventive Medicine

The Board of Trustees of the American Board of Preventive Medicine, at its annual meeting held in Philadelphia, Pa., June 4-5, 1963, reelected Dr. James H. Sterner as chairman of the board and chose Dr. John C. Hume as its new secretary-treasurer. The board requests that all inquiries, including those on eligibility requirements for examinations, fees, examination dates, and requirements for certification, be addressed to: Dr. John C. Hume, M.D., Secretary-Treasurer, American Board of Preventive Medicine, Inc., 615 N. Wolfe Street, Baltimore, Md.

November 30, 1963, is the final date for filing applications for the 1964 examinations for certification as Diplomates in Public Health, Occupational Medicine, and General Preventive Medicine, the board announced.

Dates, or probable dates and locations for the examinations are:

Public Health, March 19-21, 1964 (probable dates), at school of public health of applicant's choice.

Occupational Medicine, April 11-13, 1964, at Pittsburgh, Pa. (in conjunction with the annual meeting of the Industrial Medical Association).

General Preventive Medicine, part I (written examination), March 19-21, 1964 (prob-

able dates), at school of public health of applicant's choice. (Part II, oral, for those who successfully completed part I, is being held November 9, 1963, at the Muehlebach Hotel, Kansas City, Mo., immediately preceding and in conjunction with the annual meeting of the American Public Health Association, November 11-15, 1963, but date for filing is past.)

The board of trustees certified the following physicians:

Diplomates in Public Health: Thomas H. Lamson, John B. Atwater, Elton Kessel, Gordon S. Siegel, Robert M. Worth, Jack C. Robertson, Hope H. Corey, Richard L. Wenzel, Donald T. Rice, George L. Harper, Elizabeth Jolly, Willard R. Brown, Harry H. Levine, Ian McLaren, William S. Haynes, George E. Leone, and James A. Finger.

Diplomates in Occupational Medicine: Julian Alexander, Stanley M. Awramik, Joe D. Bentz, Earl M. Best, Jr., Marcus B. Bond, Robert E. Brubaker, Peter Carmichael, John M. Colthart, Marshall J. Hanley, Wilbert J. Helzlsouer, William A. Hogg, Thomas A. Lincoln, John MacIver, William E. O'Hara, Francis L. Purcell, Joseph B. Ruffin, and David J. Smith.